In re Application of
Tsien et al.
Filed: January 25, 2002

PATENT
Attorney Docket No. REGEN1260-3

Page 2

I. AMENDMENTS

IN THE DRAWINGS

Please enter Substitute Figure 1B and Substitute Figure 2.

IN THE SPECIFICATION

Please delete the sentence at page 1, lines 3-4, and substitute therefor:

--This application is a continuation of U.S. Serial No. 09/396,003, filed September 13, 1999, which is a continuation of U.S. Serial No. 08/792,553, filed January 31, 1997 (now U.S. Patent No. 5,981,200), which is a continuation-in-part of U.S. Serial No. 08/594,575, filed January 31, 1996.--

IN THE CLAIMS

Please cancel claims 1 to 56.

Please add new claims 57 to 78 as follows:

--57. A tandem fluorescent protein construct, comprising a donor fluorescent protein moiety, an acceptor fluorescent protein moiety and a linker moiety that couples the donor and acceptor moieties and wherein the donor and acceptor moieties exhibit fluorescence resonance energy transfer ("FRET") when the donor moiety is excited by radiation, characterized in that the linker moiety comprises a protease cleavage recognition site, wherein cleavage of the linker by a protease results in a change in FRET between the donor and acceptor moieties,

and wherein the donor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

- a) Phe64Leu, Ser65Thr, Tyr66Trp, Asn146Ile, Met153Thr, Val163A and Asn212Lys, or
- b) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or
- c) Tyr66His and Tyr145Phe, or
- d) Tyr66Trp, Asn146Ile, Met153Thr, Val163Ala and Asn212Lys, or
- e) Ser72Ala, Tyr145Phe and Thr203Ile, or
- f) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr, and